

Supplementary Materials

Corticosteroid sensitivity assays

U937 cells were pretreated with 2 μ M cryptotanshinone (MedChemExpress, State of New Jersey, USA) for 4 h and incubated with 0.5% CSE for another 2 h. Cells were seeded in 96-well plates in the presence of different concentrations of dexamethasone (10^{-11} to 10^{-6} M) (Shiyao Yinhu Pharmaceutical Co., Ltd, Hubei, China) for 1 h before overnight (16 ± 2 hr) stimulation with 10 ng/ml TNF α (Pepro Tech, State of New Jersey, USA). Supernatants were collected, and IL-8 level was measured by enzyme-linked immunosorbent assay (ELISA) (Anhui Qiaoyi Biotechnology Co., Ltd, Anhui, China). The percentage of inhibition of IL8 by dexamethasone was calculated, and corticosteroid sensitivity was measured as IC₃₀ (dexamethasone concentration inducing 30% inhibition of tumor necrosis factor- α -induced IL8 production in peripheral blood mononuclear cell), EC₅₀ (dexamethasone dose inducing inhibition halfway between minimal and maximal inhibition), E_{max} (percentage inhibition at maximal concentration).

PBMCs were pretreated with 2 μ M cryptotanshinone (CPT) for 4 h, and corticosteroid sensitivity was measured using the same method except for usage of CSE and a lower concentration of TNF α (1 ng/ml).

Supplementary Figure Legends

Figure 1. This study was conducted under the approval of the Ethics Committee of the Affiliated Huai'an Hospital of Xuzhou Medical University.

淮安市第二人民医院伦理委员会审批件

项目名称	隐丹参酮通过抑制 PI3K δ /Akt 通路改善慢性阻塞性肺疾病患者的糖皮质激素敏感性		
技术项目负责人	万玉峰	职称	主任医师
科别	呼吸与危重症医学科		
评审意见	我院医学伦理委员会经过讨论，以《纽伦堡法典》、《赫尔辛基宣言》、世界卫生组织的有关文献为指导，一致认为《隐丹参酮通过抑制 PI3K δ /Akt 通路改善慢性阻塞性肺疾病患者的糖皮质激素敏感性》没有违背有关伦理道德规范、国际准则、政策法规，院医学伦理委员会同意开展《隐丹参酮通过抑制 PI3K δ /Akt 通路改善慢性阻塞性肺疾病患者的糖皮质激素敏感性》研究。临床应用过程中项目组须严格按照技术规范，并贯彻知情同意和保密原则，患者按照有关规定，自愿签署知情同意书。		
投票结果	结论： <input checked="" type="checkbox"/> 同意 <input type="checkbox"/> 作必要修改后同意 <input type="checkbox"/> 不同意		
日期： 2021-09-30 淮安市第二人民医院伦理委员会（盖章）			

Supplementary Figure Legends

Figure 1. An English translation of the ethics approval.

Approval Document of the Ethics Committee of Huai'an Hospital Affiliated to Xuzhou Medical University			
Project name	Cryptotanshinone reverses corticosteroid insensitivity by inhibition of phosphoinositide-3-kinase- δ in chronic obstructive pulmonary disease		
Technical Project Leader	Yufeng Wan	Professional ranks and titles	Chief physician
Department	Department of Respiratory and Critical Care Medicine		
Review comments	After discussion, the Medical Ethics Committee of our hospital, guided by the Nuremberg Code, the Declaration of Helsinki and the relevant literature of the World Health Organization, agreed that the study "cryptotanshinone reverses corticosteroid insensitivity by inhibition of phosphoinositide-3-kinase- δ in chronic obstructive pulmonary disease" does not violate the relevant ethical norms, international norms, policies and regulations. The Medical Ethics Committee agreed to conduct the study "cryptotanshinone reverses corticosteroid insensitivity by inhibition of phosphoinositide-3-kinase- δ in chronic obstructive pulmonary disease". In the process of clinical application, the project team shall strictly follow the technical operation specifications, and implement the principles of informed consent and confidentiality. Patients shall voluntarily sign informed consent in accordance with relevant regulations.		
Poll results	Conclusion: <input checked="" type="checkbox"/> agree <input type="checkbox"/> agree after making necessary modifications <input type="checkbox"/> disagree		
Date: 2021-09-30			
Ethics Committee of Huai'an Hospital Affiliated to Xuzhou Medical University (seal)			